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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,079	10/22/2003	Luc Mercken	FRAV2002/0030 US NP	2372

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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
04/08/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/691,079	MERCKEN ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,9 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7,9 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 3 February 2009 have been entered. Claims 1, 6 - 7, 9, and 16 are pending and under examination.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3 February 2009 has been entered.

Withdrawn Rejections and Objections

3. The following objections and rejections set forth in the previous office action are withdrawn:

A. The objection to the specification for reciting new matter is withdrawn in light of the amendments to the specification filed 3 December 2008 and 3 February 2009.

B. The rejection under 35 USC 112, first paragraph is withdrawn in light of the amendments.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6 - 7, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for performing the active steps recited in claim 1 (i.e., steps a through e), does not reasonably provide enablement for identifying those compounds which increase production of Aβ as therapeutics for Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors

include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The examiner concedes that it is well within the skill of an artisan in this field to perform steps a) through e) of claim 1. There are no enablement issues with respect to providing cells expressing Src, introducing APP, contacting cells with candidate compounds, measuring the production of Aβ, and comparing this result to the control recited in claim 1. However, agents which increase production of Aβ would not reasonably be suitable candidates for treatment of Alzheimer's disease, as recited in claim 1 part f). The specification discloses (p. 2 lines 9 - 24 for example) that Aβ plays a "central role" in Alzheimer's disease, and points to prior art references indicating that mutations in the APP gene present in the familial forms of the disease lead to higher amounts of Aβ production *in vitro*. According to the specification, Aβ itself is toxic (p. 2 lines 9 - 12). The specification provides no working examples of identifying therapeutics for Alzheimer's disease which increase production of Aβ and offers no guidance as to how increasing Aβ production would be therapeutic.

At the time the invention was made, the prior art recognized that *in vivo*, treatments which decrease the amount of Aβ lead to decreases in the number of Alzheimer's-like plaques and improvements in cognition; see for example Bard 2000 (Nature Medicine 6:916-919), who teaches that antibodies against Aβ decrease the amount of toxic amyloid in the brain. See also Dovey 2001 (Journal of Neurochemistry 76:173-181), who teaches that molecules which inhibit Aβ production by decreasing γ-secretase activity are potential therapeutics for Alzheimer's disease. Thus the invention of claim 1, which is a method of identifying therapeutics for Alzheimer's disease by identifying molecules that increase Aβ production, stands in opposition to what was known in the art, namely that decreasing Aβ production would be expected to be therapeutic. Given that the specification provides no working examples of identifying agents which increase Aβ production that are also therapeutics for Alzheimer's disease, a large degree of experimentation would be required in order to overcome the art-recognized obstacles to treatment by increasing production of toxic Aβ. Coupled with the lack of guidance in the specification on how to do this, the large degree of experimentation required would be undue. Since the skilled artisan could not perform the method of claim 1 in the absence of undue

experimentation, the claim does not comply with the requirements of 35 USC 112, first paragraph. Claims 6 - 7 and 9 are included in this rejection as they depend from claim 1 but are not limited to embodiments which could be practiced in the absence of undue experimentation.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6 - 7, 9, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing because the steps are drawn to a method of identifying agents which increase production of Aβ, but the goal as recited in the preamble and in part f) of the method is to identify agents which are therapeutic for Alzheimer's disease. Since Aβ is toxic and is disclosed at p. 2 of the specification as playing a crucial role in the etiology of this disease, it is confusing as to how performing the steps of the method will lead to identification of a therapeutic for Alzheimer's. The claim is confusing because it is unclear whether it is a method to identify agents which increase production of Aβ and would *exacerbate* Alzheimer's disease, as would occur if steps a) through e) were followed, or if it is a method to identify therapeutics for Alzheimer's as recited in the preamble. Claims 6 - 7 and 9 are included in this rejection as they depend from claim 1 but do not clarify the scope of patent protection sought.

Claim 16 is confusing because it is unclear whether it requires the presence of SRC protein, a nucleic acid that encodes SRC protein, or both. The claim requires the step of "providing a Src protein using a Src encoding DNA". This is confusing because a skilled artisan could not determine what components are actually required for the claimed method. Is a recombinant protein required? Must the Src-encoding DNA be present? Or is "using a Src encoding DNA" merely a product-by-process limitation describing one possible way to obtain Src protein?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Abdel-Ghany 1990 (Proc Natl Acad Sci USA 87:7061-7065).

Abdel-Ghany teaches obtaining Src protein by thawing frozen insect cells transformed with genes (that is, DNA) encoding c-src and v-src. See p. 7061, second column, first complete paragraph which describes the nucleic-acid-containing cells, and paragraph beginning at the bottom of p. 7061 for protocol to obtain purified Src kinases. The DNAs encoding Src proteins are necessarily under control of an expression element, otherwise the proteins would not be expressed. Abdel-Ghany also teaches exposing the Src proteins to several candidate inhibitors, and determining which compounds inhibit Src activity. See for example p. 7062 second column first complete paragraph, which shows that phosphorylation of poly(E_4Y_1) by Src was inhibited 60% by the compound groEL. See also p. 7063 second column, the section entitled "Inhibitors and Stimulators of c-src kinase with poly(E_4Y_1) as Substrate", which describes a series of experiments in which various compounds were tested for their ability to act as inhibitors of Src activity. Note results are presented in Tables 4 and 5. As the reference by Abdel-Ghany teaches every starting material and step recited in claim 16, this claim is anticiapted.

Conclusion

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
April 1, 2009